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<p>(51) International Patent Classification ⁷ : C07K 14/505, 38/18, A61P 7/06, C12N 5/10, 15/12</p>	<p>A3</p>	<p>(11) International Publication Number: WO 00/24893 (43) International Publication Date: 4 May 2000 (04.05.00)</p>
<p>(21) International Application Number: PCT/US99/24435 (22) International Filing Date: 18 October 1999 (18.10.99) (30) Priority Data: 09/178,292 23 October 1998 (23.10.98) US (71) Applicant: AMGEN INC. [US/US]; One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US). (72) Inventors: EGRIE, Joan, C.; 561 Dos Vientos Drive, Newbury Park, CA 91320 (US). ELLIOTT, Steven, G.; 1040 Golden Crest Avenue, Newbury Park, CA 91320 (US). BROWN, Jeffrey, K.; 1244 Calle Aurora, Camarillo, CA 93010 (US). (74) Agents: ODRE, Steven, M. et al.; Amgen, Inc., One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US).</p>	<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 14 September 2000 (14.09.00)</p>	
<p>(54) Title: METHODS AND COMPOSITIONS FOR THE PREVENTION AND TREATMENT OF ANEMIA (57) Abstract Methods for increasing and maintaining hematocrit in a mammal comprising administering a hyperglycosylated analog of erythropoietin are disclosed. An analog may be administered less frequently than an equivalent molar amount of recombinant human erythropoietin to obtain a comparable target hematocrit and treat anemia. Alternatively, a lower molar amount of a hyperglycosylated analog may be administered to obtain a comparable target hematocrit and treat anemia. Also disclosed are new hyperglycosylated erythropoietin analogs, methods of production of the analogs, and compositions comprising the analogs.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K14/505 A61K38/18 A61P7/06 C12N5/10 C12N15/12		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 05465 A (AMGEN INC) 23 February 1995 (1995-02-23) cited in the application claims 1-7,9,17,19,22,23	23-32
A	claim 10; tables 3,5,6	1-22
X	WO 91 05867 A (AMGEN INC) 2 May 1991 (1991-05-02) cited in the application claims 2,5,9,10	23-32
X	EP 0 267 678 A (INTEGRATED GENETICS INC) 18 May 1988 (1988-05-18) page 1, line 9 - line 17; claims 1-6	23-32
-/-		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "A" document member of the same patent family		
Date of the actual completion of the international search 28 April 2000		Date of mailing of the international search report 17/05/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Teyssier, B

INTERNATIONAL SEARCH REPORT

Int. Patent Application No
PCT/US 99/24435

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 541 458 A (HIRST B MARK) 30 July 1996 (1996-07-30) column 6, line 14 - line 22 column 8, line 14 - line 23 claims 5,6,14,15,17-21	1-22, 31-37
A	US 5 716 644 A (BRICKNER AVRAM ET AL) 10 February 1998 (1998-02-10) column 1, line 23 - line 48	1-22, 31-37
A	FIBI M R ET AL: "N- AND O-GLYCOSYLATION MUTAINS OF RECOMBINANT HUMAN ERYTHROPOIETIN SECRETED FROM BHK-21CELLS" BLOOD, vol. 85, no. 5, 1 March 1995 (1995-03-01), pages 1229-1236, XP002053700 page 1235, last paragraph	1-37
A	EGRIE J C ET AL.: "The role of carbohydrate on the biological activity of erythropoietin" GLYCOCONJUGATE JOURNAL, 15 - 20 August 1993, page 263 XP000906829 Abstracts of XIIth International Symposium cited in the application	
A	ELLIOTT STEVE ET AL.: "Structural requirements for addition of O-linked carbohydrate to recombinant erythropoietin." BIOCHEMISTRY, vol. 33, no. 37, 17 September 1994 (1994-09-17), pages 11237-11245, XP000906783	
P,X	WO 99 11781 A (FIBI MATHIAS ;HERMENTIN PETER (DE); HOECHST MARION ROUSSEL DE GMBH) 11 March 1999 (1999-03-11) claims 1-5,8-10,12,14-19,22	23-31

INTERNATIONAL SEARCH REPORT

International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-22 and 32-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: 1, 7, 33, 35
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.:
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 7, 33, 35

Present claims 1 and 33 on one hand and 7 and 35 on the other hand relate to the administration of compounds characterised (inter alia) by reference to the frequency and dose of administration, respectively. In this context, the wordings "less frequently" and "lower molar amount" with reference to prior art recombinant human EPO were not considered clear within the meaning of Article 6 PCT. Consequently, with respect to claims 2, 8, 34, 36 and line 14, page 4 of the description, the search has been restricted to "two times a week or less" (claim 1) or "one time a week or less" (claim 33) and "total molar amount of less than of 4.5 mug/kg/week or 150 units/kg/week" (claims 7, 35), respectively.

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9505465 A	23-02-1995	AT 155796 T	15-08-1997
		AU 677097 B	10-04-1997
		AU 7632794 A	14-03-1995
		CN 1105030 A	12-07-1995
		CZ 9500917 A	13-03-1996
		DE 69404401 D	04-09-1997
		DE 69404401 T	19-02-1998
		DK 640619 T	02-02-1998
		EP 0640619 A	01-03-1995
		ES 2105442 T	16-10-1997
		FI 951792 A	18-05-1995
		GR 3024815 T	30-01-1998
		HK 1001589 A	26-06-1998
		HU 72849 A	28-05-1996
		JP 11155584 A	15-06-1999
		JP 2938572 B	23-08-1999
		JP 8506023 T	02-07-1996
		LV 10972 A	20-12-1995
		LV 10972 B	20-10-1996
		NO 951445 A	16-06-1995
		NZ 273134 A	24-11-1997
		SI 640619 T	28-02-1998
		SK 50295 A	09-08-1995
		ZA 9406122 A	20-03-1995
WO 9105867 A	02-05-1991	AT 146187 T	15-12-1996
		AT 184914 T	15-10-1999
		AU 646822 B	10-03-1994
		AU 6604290 A	16-05-1991
		CA 2027635 A	14-04-1991
		CA 2165694 A	14-04-1991
		CN 1051936 A	05-06-1991
		DE 69029370 D	23-01-1997
		DE 69029370 T	05-06-1997
		DE 69033301 D	28-10-1999
		DE 69033301 T	20-04-2000
		DK 428267 T	09-06-1997
		EP 0428267 A	22-05-1991
		EP 0668351 A	23-08-1995
		ES 2097753 T	16-04-1997
		FI 964648 A	21-11-1996
		GR 3022658 T	31-05-1997
		HK 1006718 A	12-03-1999
		JP 8151398 A	11-06-1996
		JP 2983629 B	29-11-1999
		JP 4502331 T	23-04-1992
		NO 301832 B	15-12-1997
		NZ 235676 A	28-04-1992
		PT 95586 A, B	30-09-1991
US 5856298 A	05-01-1999		
ZA 9008166 A	28-08-1991		
EP 0267678 A	18-05-1988	US 4954437 A	04-09-1990
		AU 7842987 A	16-03-1989
		DK 478287 A	16-03-1988
		FI 873897 A	16-03-1988
		JP 63185396 A	30-07-1988
		PT 85699 A, B	01-10-1987

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/24435

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5541458 A	30-07-1996	EP 0712207 A	15-05-1996
		JP 8256478 A	01-10-1996
US 5716644 A	10-02-1998	AU 705451 B	20-05-1999
		AU 5972496 A	30-12-1996
		AU 705968 B	03-06-1999
		AU 6034196 A	30-12-1996
		CA 2223583 A	19-12-1996
		CA 2223834 A	19-12-1996
		CZ 9703908 A	13-05-1998
		EP 0871433 A	21-10-1998
		EP 0831786 A	01-04-1998
		JP 11506764 T	15-06-1999
		NZ 309533 A	30-08-1999
		PL 323736 A	14-04-1998
		WO 9640073 A	19-12-1996
		WO 9640074 A	19-12-1996
		AU 698016 B	22-10-1998
		AU 4275597 A	15-01-1998
		AU 680422 B	31-07-1997
		AU 4630893 A	04-01-1994
		CA 2136434 A	23-12-1993
		EP 0644771 A	29-03-1995
		JP 7507806 T	31-08-1995
		WO 9325221 A	23-12-1993
US 5674534 A	07-10-1997		
WO 9911781 A	11-03-1999	EP 0902085 A	17-03-1999
		AU 9533798 A	22-03-1999